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Animal Models Information Center

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What have we learned from animal models of aging about age-related diseases such as cancer?

Mice are excellent models for cancer research. They are mammals and thus genetically similar to humans. They develop many of the same cancers that we do, and they can be induced to develop others by exposures to cancer-causing substances. Researchers have bred various strains of mice with particular characteristics that make them especially good models for human disease. Some of the useful strains include:

- Transgenic mice: These mice have had a gene or genes inserted into their DNA and thus have been genetically engineered to develop a disease such as breast cancer.

- Immunodeficient mice: These have immune deficiencies (one strain is the nude mouse), and they are used to study cancer and AIDS, among other diseases.

- Knockout mice: These mice have been engineered to lack specific genes.

In recent years, our understanding of the genetic basis of many cancers has been refined. Humans carry some genes that induce cancers (oncogenes) and others that suppress cancers (tumor suppressor genes). A number of mouse strains have been bred that carry either human oncogenes or suppressor genes. Mice with human oncogenes such as those for breast cancer will reliably develop the disease, and thus they provide a useful model for an understanding of the disease and for testing potential treatments. Mice have also been bred to lack their tumor suppressor genes, and these mice have been found to be particularly susceptible to the development of cancer.

Some of the human cancers for which we have useful mouse models for study include:

- Breast cancer: Human breast cancer is believed to be related to multiple factors, including mutations in oncogenes that permit them to be expressed and mutations in suppressor genes that prevent them from being expressed. Transgenic mice have been bred that possess high levels of some of the oncogenes and

knockout mice have been bred that are missing key genes. While the various strains have been used extensively to elucidate the pathology of breast cancer and to test various treatments, scientists are now looking to create "designer" mice that combine some of the different gene abnormalities of human breast cancer to more fully understand the disease.

- Colorectal cancer: Cancer of the colon and rectum is one of the most commonly occurring human cancers, and its incidence is apparently rising. Animal models for colorectal cancers have been unsatisfying to date, but efforts are ongoing to develop specially bred rodent models. Mice that have mutations in the gene called Smad3 are born fertile and viable, but between 4 and 6 months of age, they develop metastatic colon cancer. This cancer is related to the activity of tumor growth factors, and the researchers working with these mice are optimistic that they will provide a good model for studying human colorectal cancers.

- Prostate cancer: Significant effort has been made in the research community to develop a useful animal model for prostate cancer. About 25 nude mouse strains have been bred. They manifest different aspects of prostate cancer, from early progression of the disease to the effects of male hormones on it.